



dopamine transporter deficiency syndrome

Dopamine transporter deficiency syndrome is a rare movement disorder. The condition is also known as infantile parkinsonism-dystonia because the problems with movement (dystonia and parkinsonism, described below) usually start in infancy and worsen over time. However, the features of the condition sometimes do not appear until childhood or later.

People with dopamine transporter deficiency syndrome develop a pattern of involuntary, sustained muscle contractions known as dystonia. The dystonia is widespread (generalized), affecting many different muscles. The continuous muscle cramping and spasms cause difficulty with basic activities, including speaking, eating, drinking, picking up objects, and walking.

As the condition worsens, affected individuals develop parkinsonism, which is a group of movement abnormalities including tremors, unusually slow movement (bradykinesia), rigidity, and an inability to hold the body upright and balanced (postural instability). Other signs and symptoms that can develop include abnormal eye movements; reduced facial expression (hypomimia); disturbed sleep; frequent episodes of pneumonia; and problems with the digestive system, including a backflow of acidic stomach contents into the esophagus (gastroesophageal reflux) and constipation.

People with dopamine transporter deficiency syndrome may have a shortened lifespan, although the long-term effects of this condition are not fully understood. Children with this condition have died from pneumonia and breathing problems. When the first signs and symptoms appear later in life, affected individuals may survive into adulthood.

Frequency

Dopamine transporter deficiency syndrome appears to be a rare disease; only about 20 affected individuals have been described in the medical literature. Researchers believe that the condition is probably underdiagnosed because its signs and symptoms overlap with cerebral palsy and other movement disorders.

Genetic Changes

Dopamine transporter deficiency syndrome is caused by mutations in the *SLC6A3* gene. This gene provides instructions for making a protein called the dopamine transporter. This protein is embedded in the membrane of certain nerve cells (neurons) in the brain, where it transports a molecule called dopamine into the cell. Dopamine is a chemical messenger (neurotransmitter) that relays signals from one neuron to another. Dopamine has many important functions, including playing complex roles in thought (cognition), motivation, behavior, and control of movement.

Mutations in the *SLC6A3* gene impair or eliminate the function of the dopamine transporter. The resulting shortage (deficiency) of functional transporter disrupts dopamine signaling in the brain. Although dopamine has a critical role in controlling movement, it is unclear how altered dopamine signaling causes the specific movement abnormalities found in people with dopamine transporter deficiency syndrome.

Studies suggest that the age at which signs and symptoms appear is related to how severely the function of the dopamine transporter is affected. Affected individuals who develop movement problems starting in infancy most often have transporter activity that is less than 5 percent of normal. Those whose movement problems appear in childhood or later tend to have somewhat higher levels of transporter activity, although they are still lower than normal. Researchers speculate that higher levels of transporter activity may delay the onset of the disease in these individuals.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- DTDS
- infantile parkinsonism-dystonia
- parkinsonism-dystonia, infantile
- PKDYS

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Infantile Parkinsonism-dystonia
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2751067/>

Other Diagnosis and Management Resources

- GeneReview: Parkinson Disease Overview
<https://www.ncbi.nlm.nih.gov/books/NBK1223>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>

- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Dystonia
<https://medlineplus.gov/dystonia.html>
- Health Topic: Parkinson's Disease
<https://medlineplus.gov/parkinsonsdisease.html>

Genetic and Rare Diseases Information Center

- Infantile Parkinsonism-dystonia
<https://rarediseases.info.nih.gov/diseases/10484/infantile-parkinsonism-dystonia>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Dystonia Fact Sheet
<https://www.ninds.nih.gov/Disorders/All-Disorders/Dystonias-Information-Page>

Educational Resources

- Disease InfoSearch: Infantile Parkinsonism-dystonia
<http://www.diseaseinfosearch.org/Infantile+Parkinsonism-dystonia/3812>
- MalaCards: parkinsonism-dystonia, infantile
http://www.malacards.org/card/parkinsonism_dystonia_infantile
- Merck Manual Consumer Version: Dystonia
<http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/movement-disorders/dystonia>
- Merck Manual Consumer Version: Parkinsonism
<http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/movement-disorders/parkinsonism>

Patient Support and Advocacy Resources

- Dystonia Medical Research Foundation
<https://www.dystonia-foundation.org/>
- National Organization for Rare Disorders: Dystonia
<https://rarediseases.org/rare-diseases/dystonia/>
- The Bachmann-Strauss Dystonia & Parkinson Foundation
<http://www.dystonia-parkinson.org/>

GeneReviews

- Parkinson Disease Overview
<https://www.ncbi.nlm.nih.gov/books/NBK1223>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28infantile+parkinsonism-dystonia%5BTIAB%5D%29+OR+%28dopamine+transporter+deficiency+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

OMIM

- PARKINSONISM-DYSTONIA, INFANTILE
<http://omim.org/entry/613135>

Sources for This Summary

- Blackstone C. Infantile parkinsonism-dystonia due to dopamine transporter gene mutations: another genetic twist. *Lancet Neurol.* 2011 Jan;10(1):24-5. doi: 10.1016/S1474-4422(10)70280-5. Epub 2010 Nov 25.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21112252>
- Blackstone C. Infantile parkinsonism-dystonia: a dopamine "transportopathy". *J Clin Invest.* 2009 Jun;119(6):1455-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19504720>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2689103/>
- Kurian MA, Li Y, Zhen J, Meyer E, Hai N, Christen HJ, Hoffmann GF, Jardine P, von Moers A, Mordekar SR, O'Callaghan F, Wassmer E, Wraige E, Dietrich C, Lewis T, Hyland K, Heales S Jr, Sanger T, Gissen P, Assmann BE, Reith ME, Maher ER. Clinical and molecular characterisation of hereditary dopamine transporter deficiency syndrome: an observational cohort and experimental study. *Lancet Neurol.* 2011 Jan;10(1):54-62. doi: 10.1016/S1474-4422(10)70269-6. Epub 2010 Nov 25.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21112253>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3002401/>

- Kurian MA, Zhen J, Cheng SY, Li Y, Mordekar SR, Jardine P, Morgan NV, Meyer E, Tee L, Pasha S, Wassmer E, Heales SJ, Gissen P, Reith ME, Maher ER. Homozygous loss-of-function mutations in the gene encoding the dopamine transporter are associated with infantile parkinsonism-dystonia. *J Clin Invest*. 2009 Jun;119(6):1595-603. doi: 10.1172/JCI39060. Epub 2009 May 26.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19478460>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2689114/>
- Ng J, Zhen J, Meyer E, Erreger K, Li Y, Kakar N, Ahmad J, Thiele H, Kubisch C, Rider NL, Morton DH, Strauss KA, Puffenberger EG, D'Agnano D, Anikster Y, Carducci C, Hyland K, Rotstein M, Leuzzi V, Borck G, Reith ME, Kurian MA. Dopamine transporter deficiency syndrome: phenotypic spectrum from infancy to adulthood. *Brain*. 2014 Apr;137(Pt 4):1107-19. doi: 10.1093/brain/awu022. Epub 2014 Mar 10.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24613933>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3959557/>

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/dopamine-transporter-deficiency-syndrome>

Reviewed: October 2015

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services